

CLAIMS

1. An attenuated bovine viral diarrhea (BVD) virus, wherein said virus carries in the viral genome, a mutated N^{pro} coding sequence comprising an intact 5' region, and a sequence coding for a monomeric bovine ubiquitin, wherein the ubiquitin coding sequence is operably placed between the 3' end of said mutated N^{pro} coding sequence and the 5' end of the coding sequence for the viral core protein.
2. The attenuated BVD virus of claim 1, comprising a genomic nucleic acid sequence as set forth in SEQ ID NO: 11, or a degenerate variant thereof.
3. The attenuated BVD virus of claim 1, comprising a genomic nucleic acid sequence essentially as set forth in SEQ ID NO: 11, or a degenerate variant thereof.
4. An isolated nucleic acid molecule comprising the genomic sequence of an attenuated BVD virus, wherein said virus carries in the viral genome, a mutated N^{pro} coding sequence comprising an intact 5' region, and a sequence coding for a monomeric bovine ubiquitin, wherein the ubiquitin coding sequence is operably placed between the 3' end of said mutated N^{pro} coding sequence and the 5' end of the coding sequence for the viral core protein.
5. An isolated nucleic acid molecule comprising a sequence as set forth in SEQ ID NO: 11, or a degenerate variant thereof.
6. An isolated nucleic acid molecule comprising a sequence essentially as set forth in SEQ ID NO: 11, or a degenerate variant thereof.
7. A vector comprising a sequence essentially as set forth in SEQ ID NO: 11, or a degenerate variant thereof.
8. A vector designated as pBVDdN6 (ATCC No. PTA-2532) (SEQ ID NO: 12).
9. A cell transformed or transfected with any of the nucleic acid molecules of claims 4-6.
10. A cell transformed or transfected with the vector of claim 7 or 8.

11. A progeny virus produced by the cell of claim 9.

12. A progeny virus produced by the cell of claim 10.

13. A method of modifying the genomic nucleic acid molecule of an isolated wild type BVD virus, comprising introducing a mutation into the 3' region of the N^{pro} protease gene wherein said mutation renders the N^{pro} protein inactive, and inserting a sequence coding for a monomeric bovine ubiquitin between the mutated N^{pro} coding sequence and the coding sequence of the core protein. .

14. The method of claim 13, wherein said mutation in the N^{pro} protease gene comprises a deletion of about one third of the N^{pro} coding region from the 3' end.

15. A method of attenuating an isolated wild type BVD virus, comprising isolating the genomic nucleic acid molecule from said virus, introducing a mutation into the 3' region of the N^{pro} protease gene in the viral genome, wherein said mutation renders the N^{pro} protein inactive; inserting a sequence coding for a monomeric bovine ubiquitin between the mutated N^{pro} coding sequence and the coding sequence of the core protein; and producing from the modified genome an attenuated virus suitable for use in a vaccine.

16. An immunogenic composition comprising the attenuated BVD virus of any of claims 1-3 and a veterinarily-acceptable carrier.

17. An immunogenic composition comprising the isolated nucleic acid molecule of any of claims 4-6 and a veterinarily-acceptable carrier.

18. A method of inducing an immune response against BVDV in an animal subject, comprising administering an immunologically effective amount of the attenuated BVD virus of any of claims 1-3 and a veterinarily-acceptable carrier.

19. A method of inducing an immune response against BVDV in an animal subject, comprising administering an immunologically effective amount of the isolated nucleic acid molecule of any of claims 4-6.

20. The method of claim 18, wherein said immune response is a cellular or humoral immune response.

21. The method of claim 19, wherein said immune response is a cellular or humoral immune response.

22. The method of claim 18, wherein said immune response results in the production of antibodies against BVDV in said animal.

23. The method of claim 19, wherein said immune response results in the production of antibodies against BVDV in said animal.

24. A vaccine composition comprising the attenuated BVD virus of any of claims 1-3 and a veterinarily-acceptable carrier.

25. A vaccine composition comprising the isolated nucleic acid molecule of any of claims 4-6 and a veterinarily-acceptable carrier.

26. A method of treating a BVDV infection in an animal, comprising administering to said animal, a therapeutically effective amount of the attenuated BVD virus of any of claims 1-3.

27. A method of treating a BVDV infection in an animal, comprising administering to said animal, a therapeutically effective amount of the isolated nucleic acid molecule of any of claims 4-6.

28. A method of identifying a BVD virus in an animal as an attenuated BVD virus of any of claims 1-3, said animal suspected of suffering a BVDV infection, comprising isolating the virus from said animal, detecting the presence of the ubiquitin coding sequence, thereby determining the isolated virus as identical to the attenuated BVD virus of any of claims 1-3.

29. A method of identifying a BVD virus in an animal as an attenuated BVD virus of any of claims 1-3, said animal suspected of suffering a BVDV infection, comprising isolating the virus from said animal, detecting the presence of the mutation in the N^{pro} gene, thereby determining the isolated virus as identical to the attenuated BVD virus of any of claims 1-3.

09693401